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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	062587-5002	4013

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EXAMINER	
SOROUSH, LAYLA	
ART UNIT	PAPER NUMBER
1627	
MAIL DATE	DELIVERY MODE
08/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/847,538	SCHULZE ET AL.	
	Examiner	Art Unit	
	LAYLA SOROUSH	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,53-57,61,62,64,66,68,70-73 and 75-83* is/are pending in the application.

4a) Of the above claim(s) *33,53-57,61,62,64,66,68,70-73 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75-77 and 79-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed April 20, 2010 presents remarks and arguments submitted to the office action mailed January 21, 2010 is acknowledged.

Applicant's arguments over the 35 U.S.C. 102 (b) rejection of claims 58, 60, 63, 65, 67, and 69, over Kress et al. (WO 96/04017A1 (English Equivalent US Pat No. 6,048,515) is persuasive in view of cancellation of the claims. Therefore, the rejection of record is herewith withdrawn.

Applicant's arguments over the 35 U.S.C. 103 (a) rejection of claims 59, 74-77 and 79-82 over Kress et al. (WO 96/04017A1 (English Equivalent US Pat No. 6,048,515)) in view of Boehm et al. (J Pharm Belg. 2000 Mar-Apr;55(2):abstract) is not persuasive. Therefore, the rejection of record is herewith maintained.

The rejection is modified below to address the cancellation of the claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 75-77 and 79-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kress et al. (WO 96/04017A1 (English Equivalent US Pat No.

6,048,515– previously presented)) in view of Boehm et al. (J Pharm Belg. 2000 Mar-Apr;55(2)– previously presented).

Kress et al. teaches nanoparticles characterized in that they have an iron-containing core of iron or iron ions, a primary coat (synthetic polymer) and a secondary coat (target polymer), and optional auxiliary pharmaceutical substances, pharmaceuticals and/or adsorption mediators (Abstract; col 5 lines 45-46). The particles are useful as vehicles for medical substances in the field of therapeutics. The specificity of the nanoparticles is used for the transport of medical substances to their place of action. The medical substances may be incorporated in the iron-containing core or chemically bonded to the synthesis polymer and/or the targeting polymer (col 17 lines 41-47). Such medical substances are inclusive of cytostatic agents (col 18, lines 13-15) and hormones. "As the nanoparticles combine high physical quality with excellent targetability by flexible adjustment (modular design) of the targeting polymer (secondary coat) to the respective problem, they are applicable for many special indications such as MR lymphography after intravenous or local interstitial administration, tumor visualization, visualization of functions or malfunctions, of plaque (atherosclerosis imaging), thrombi and vascular occlusions, MR angiography, perfusion imaging, infarct visualization, visualization of endothelial damages, receptor imaging, visualization of blood-brain barrier integrity etc., as well as for differential diagnosis, in particular, for distinguishing tumors/metastases from hyperplastic tissue (col 16 line 49-60)." "The nanoparticles according to the invention are further characterized in that they are available in the form of stable colloidal sols,

which is preferred (col 5, lines 34-36)." "The hydrodynamic diameter of said basic structural unit (iron-containing core plus primary coat) in solution is smaller than 100 nm, preferably smaller than 50 nm, and not more than five times the diameter of the iron-containing core (col 5, lines 29-33)." "It is one of the specific advantages of the production method according to the invention that it offers great flexibility in the selection of synthesis polymers; the term "polymer" is not to be taken literally, as both low-molecular weight substances and mixtures of low- and polymolecular weight substances can be used for producing iron-containing cores. Particularly preferred is the use of low-molecular and polymolecular substances that contain negative charge carriers in their molecule (col 12 lines 1-10)." "Low-molecular weight substances such as carboxypolyalcohols, polycarboxypolyalcohols, polycarboxyalcohols, carboxyalcohols, alcohols, monosugars, oligosugars, and synthesis polymers such as polyethylene glycol, polypropylene glycol and mixtures (block and copolymers), polyacrylic acid, polyvinyl alcohol, polylactic acid (polylactide and polylactide glycide), and natural or, specifically, partially synthetic or chemically and/or enzymatically modified natural polymers such as dextrans and its derivatives, arabinic acid, glycosaminoglycan and synthetic analogues, starch and its derivatives as well as gelatin derivatives. It is particularly preferable to use low-molecular weight derivatives of dextran that contain negative charge carriers(col 12 lines 23-40)."

Kress et al. fails to teach measuring the zeta potential of the composition or measuring the isoelectric point of the composition comprising the emulsions.

Boehm et al. teaches "Colloidal drug carriers which mainly involve submicron emulsions, nanoparticles, microparticles, liposomes and lipid complexes have received increasing interest in recent years mainly as vehicles of lipophilic drugs and as improved delivery systems for drug targeting. Size and encapsulation efficiency are, in general, the two parameters used to characterize these pharmaceutical forms. Nevertheless, the surface characteristics of these dispersion have been known to influence their physical, chemical and biological properties. Then, the aim of these study is to evaluate, with some examples and illustrations, the interest of zeta potential determinations to improve the characterization of these colloidal drug carriers (abstract)."

Hence, one of ordinary skill in the art at the time of the invention when dealing with colloidal drug carriers would determine the zeta potential of the composition in order to determine surface characteristics of the dispersion for improving the colloidal drug carrier. The motivation is because one would have had a reasonable expectation of success in achieving the safest clinical outcome.

Additionally, since the "cationic agents" by definition must have a isoelectric point above 7 (see instant specification, pg. 15, at para 0057), absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize such parameters during the processes described by either Kress et al. by routine experimentations. The ordinary skill in the art would have been motivated to do such optimization to improve stability and delivery of such systems.

Applicant is informed that a prior art composition that comprise all elemental components of the instantly created composition would meet all functional characteristics of the created composition, because such characteristics are inseparable from the composition. Kress et al. meets all elemental steps of the instant claims and the compositions created thereof. Since Kress et al.'s compositions are prepared by the same steps as the instantly claimed process and further comprise all elemental components of the instantly prepared composition, they would obviously exhibit the same zeta potentials, isoelectric point, and targeting properties as those instantly claimed, because such functional characteristics of the created composition is inseparable from the describe composition of Kress et al.

Response to Arguments

Applicants argues the Kresse reference fails to measuring the zeta potential of the composition or measuring the isoelectric point of the composition comprising the emulsions. Examiner points that the 35 U.S.C. 103 obviousness type rejection is made further in view of Boehm et al. The secondary reference clearly provides motivation to measure the zeta potential or the isoelectric point of a composition comprising an emulsion. More specifically, Boehm et al. teaches when dealing with colloidal drug carriers one would determine the zeta potential of the composition in order to determine surface characteristics of the dispersion for improving the colloidal drug carrier. Additionally, applicants

argument that the Boehm et al. reference "seems to suggest that associating an active agent with cationic component may result in an unstable composition" is speculative at best; since the reference is clearly pointing to a specific study and there is no evidence of record that would negate the motivation to measure the zeta potential or the isoelectric point of a composition specifically to determine surface characteristics of the dispersion for improving the colloidal drug carrier.

Lastly, the Examiner states that although the Thode reference teaches various batches of carboxydextran coated iron oxide particles having a negative zeta potential, not all the particles of Kress et al. are carboxydextran and will have a negative zeta potential. The reference, also, generally reads on a dextran which is positively charged. Therefore, Applicants arguments that the Kress et al. reference particles all have a negative zeta potential is not persuasive.

The arguments are not persuasive and the rejection is made **FINAL**.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627